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Severe babesiosis with associated splenic infarcts and asplenia

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ABSTRACT

We describe two patients who presented with severe autoimmune hemolytic anemia in the setting of babesiosis. Notably, one patient was immunocompetent but was found to have splenic infarcts of uncertain duration, while the other patient developed disease in the context of asplenia secondary to prior surgical removal of the spleen. Both patients received antibiotics and transfusion support and eventually made a full recovery. While the patient in case 1 had parasitemia >10%, neither patient ultimately required therapeutic red blood cell exchange transfusion during the course of their respective hospitalizations. Our two cases emphasize the importance of recognizing the hemolytic anemia component of this potentially life-threatening infection, and the importance of rapidly initiating treatment in these complex clinical situations.

KEYWORDS Autoimmune hemolytic anemia; *Babesia microti*; babesiosis; parasitemia; splenic infarcts

Babesia microti, the infectious organism responsible for clinical babesiosis, is transmitted by the *Ixodes* tick. Here we present one case of severe babesiosis with a parasite load >10% in an immunocompetent host and a second case of warm autoimmune hemolytic anemia in an immunocompromised host with a parasite load <10%. Severe *Babesia* infection in immunocompetent adults without a predisposing condition is rare.[1–3] There is increasing recognition of *Babesia* infections and related complications,[4,5] and a clear mechanistic etiology and treatment optimization will be critical to improve outcomes.

CASE 1

A 63-year-old man with hyperlipidemia presented with a 1-week history of poor appetite, nausea, and nasal stuffiness concerning for coronavirus disease 2019 pneumonia. Testing for SARS-CoV-2 was negative, but he was febrile (temperature 100.5°F), hypotensive, and hypoxic with a 2 L oxygen requirement. Initial laboratory tests were significant for a platelet count of 41,000/μL, total bilirubin of 2.4 mg/dL, and ferritin of 4223 ng/mL *(Table 1)*. Computed tomography (CT) of the chest, abdomen, and pelvis showed a small left pleural effusion and splenic infarcts with possible splenic pseudoaneurysm *(Figure 1)*. Evaluation of the peripheral blood film revealed intraerythrocytic inclusions consistent with *Babesia*. Repeat evaluation demonstrated an increase in his parasitemia (6.6% to 12.9%) over a 24-hour period. The patient was initiated on atovaquone, azithromycin, and doxycycline and transferred to our center for consideration of therapeutic red blood cell (RBC) exchange transfusion.

On presentation to our center, the patient was afebrile and normotensive, but remained hypoxic with a 2 L oxygen requirement. He reported fatigue, diffuse myalgias, mild dyspnea on exertion, and dark urine for 1 week prior to his initial presentation. He had not noticed any tick bites, but reported that he was an active golfer and often walked along wooded areas on the golf course. His laboratory evaluation included a normal fibrinogen, a negative direct antiglobulin test (DAT), and urinalysis with 1+ blood and 0–2 RBC *(Table 1)*. Clindamycin was added to the patient's antibiotic regimen with reduction of parasitemia to 3.4% the following day. Thrombocytopenia was thought to be secondary to babesiosis and recovered over 1 week. Therapeutic RBC exchange transfusion was deferred, and he completed a

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Table 1. Pertinent laboratory values at initial presentation as well as upon initial presentation to our facility

	Case 1		Case 2	
Laboratory test	First hospital	MGH	First hospital	MGH
White blood cells (1000/μL)	5.7	5.3	15.9	16.8
Hemoglobin (g/dL)	11.2	7.1	2.2	4.8
Platelets (1000/μL)	41	59	347	296
Aspartate transaminase (U/L)	113	93	829	640
Alanine aminotransferase (U/L)	49	41	168	130
Alkaline phosphatase (U/L)		42	57	59
Total bilirubin (mg/dL)	2.4	1.3	5.4	8.2
Direct bilirubin (mg/dL)		0.5	2.6	4.3
Ferritin (μg/L)	4223			7702
Lactate dehydrogenase (U/L)		792	>2500	4131
Haptoglobin (mg/dL)		<10		<10

MGH indicates Massachusetts General Hospital.

14-day course of azithromycin and atovaquone plus a 21-day course of doxycycline with symptom resolution.

CASE 2

A 48-year-old man presented with 1 week of generalized weakness, fatigue, dyspnea, confusion, and dizziness in the setting of recent travel to Martha's Vineyard. He had a history of gastrointestinal stromal tumor (diagnosed at age 42) successfully treated with chemotherapy followed by surgical resection, which included splenectomy. His hemoglobin was 2.2 g/dL at presentation, with a positive DAT (IgG 4+, C3 3+), positive Lyme IgM, and a peripheral smear showing *Babesia* with a parasitemia of 1.6%. He was started on atovaquone and azithromycin, received 7 units of RBCs, and was transferred to our center for consideration of therapeutic RBC exchange transfusion.

On arrival, he had 23% reticulocytes and a positive DAT *(Table 1)*. Peripheral smear showed a large number of nucleated RBCs and Howell-Jolly bodies. Therapeutic RBC exchange was deferred given his low parasitemia (<10%), and he was treated for 4 days with dexamethasone 40 mg for autoimmune hemolytic anemia. He was discharged on a 6-week prednisone taper, 6-week course of atovaquone and azithromycin, and 3-week course of doxycycline (for Lyme coinfection).

DISCUSSION

We present two unusual cases of clinically significant babesiosis. While others have reported severe *Babesia* infection in immunocompetent adults,[1–3] our first patient's disease severity was surprising given the lack of Lyme coinfection.[3,6] Further, the combination of splenic infarcts,[7,8] hemolytic anemia,[9] and thrombocytopenia in a single host has yet to be reported.

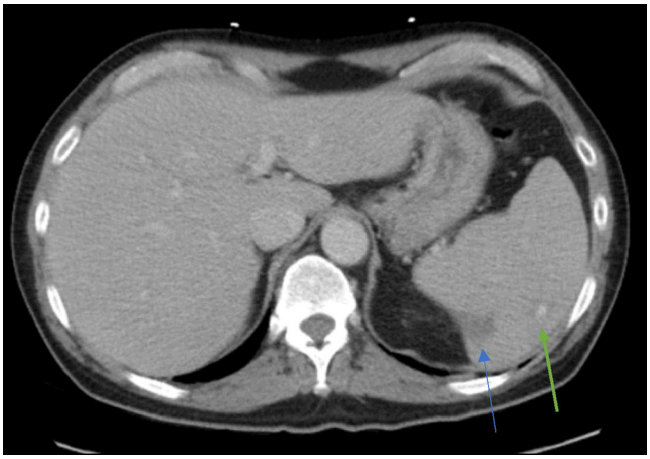

Figure 1. Case 1: CT of the abdomen notable for splenomegaly with wedge-shaped multifocal hypodensities (blue arrow) throughout—new findings compared with prior imaging studies. There is a 2.3 × 1.4 cm avidly enhancing area in the inferior aspect of the spleen (green arrow), which is new when compared to the prior exam, suggestive of a pseudoaneurysm or small acute hemorrhage.

While splenic infarction in cases of systemic babesiosis infection has been reported,[7,8] there is no clear mechanistic explanation.[7] In our first case, it is fair to question whether the multiple splenic infarcts were simply the result of his serious *Babesia* infection. Unlike reported cases of splenic rupture,[10] splenic infarcts seem to be related to the extent of parasitemia and comorbid conditions.[7,8] Further mechanistic delineation may be beneficial for therapeutic optimization in patients with severe babesiosis; however, this may be challenging given that splenic infarcts associated with other infections (e.g., mononucleosis) tend to be rare.[11–13]

The decision to defer therapeutic RBC exchange was based on the patient's clinical stability, lack of comorbid risk factors, and improvement on antibiotics.[14] Exchange transfusion is suggested to be of the highest therapeutic benefit in cases of high parasite load[15] and may mitigate the risk of acute disseminated intravascular coagulation for parasitemia >10%.[16]

Given the known risk of warm autoimmune hemolytic anemia in patients without a spleen[17] and lack of alternative explanation, our second patient's hemolytic anemia was attributed to ongoing *Babesia* infection. Further work is needed to evaluate the mechanism of this *Babesia*-related autoimmune hemolysis, especially given the report of cases in the setting of an undetectable parasitemia despite ongoing hemolysis.[17] Whether this antibody-mediated hemolysis targets antigens present on all RBCs, or the target antigens are present exclusively on *infected* RBCs, may have implications for future treatment regimens.

Therapeutic RBC exchange transfusion has been shown to be beneficial as an adjunct therapy, and there have been recent efforts to further identify specific indications.[18] It has been shown that early exchange transfusion has benefits, but

it is unclear when in the course to initiate this therapy. While treatment options warrant nuanced, individualized discussion, there is a need for evidence-based indications for appropriate use of therapeutic RBC exchange transfusion as an adjunct therapy for *Babesia* infection.

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